Article

Single intramural leiomyoma with normal hysteroscopic findings does not affect ICSI–embryo transfer outcome

Gurkan Bozdag, MD, is a specialist at the Department of Obstetrics and Gynecology, School of Medicine, Hacettepe University, Ankara. Following medical school and residency training at Ankara and Hacettepe University, he obtained a clinical fellowship at Hacettepe University, Division of Reproductive Endocrinology and Infertility, in 2006. His special interests are polycystic ovary syndrome, endometriosis and assisted reproductive technologies.

Dr Gurkan Bozdag

Gurkan Bozdag[1], Ibrahim Esinler, Kubra Boynukalin, Tarik Aksu, Serdar Gunalp, Timur Gurgan
Hacettepe University, School of Medicine, Department of Obstetrics and Gynecology, Ankara, Turkey
[1]Correspondence: e-mail: gbozdag@hacettepe.edu.tr

Abstract

Where there is no distortion of the endo–myometrial junction, the effect of an intramural leiomyoma on reproductive performance is controversial. The current study compared the performance of patients having a single leiomyoma and intact endometrium confirmed by hysteroscopy (study group) with that of controls having intact endometrium alone in intracytoplasmic sperm injection (ICSI) cycles. A total of 61 consecutive infertile patients were retrospectively enrolled into the study group from a computerized IVF database. The control group consisted of 444 age-matched patients undergoing ICSI–embryo transfer without any endocervical or intrauterine pathology confirmed by both transvaginal ultrasonography and office hysteroscopy. The baseline characteristics, performance of ovarian stimulation and embryological data were similar between the two groups. The clinical pregnancy per embryo transfer (36 versus 38%) and implantation rate (20 versus 19%) were also comparable. Although the miscarriage rate tended to be higher in the leiomyoma group (27 versus 19%), the difference did not reach statistical significance. In conclusion, in the presence of intact endometrium, a single intramural leiomyoma does not seem to have a deleterious effect on ICSI cycles. Before ICSI is attempted, hysteroscopy may be useful for ruling out distortion of the endometrium due to leiomyoma in selected cases.

Keywords: *hysteroscopy, intracytoplasmic sperm injection, leiomyoma, miscarriage, pregnancy*

Introduction

Uterine leiomyoma is the most common benign tumour of the pelvic organs, with an incidence of 20–40% (Klatsky *et al.*, 2008). Although most cases of leiomyoma are asymptomatic, they may be associated with menorrhagia, pelvic pain and/or urinary symptoms, depending on size, position and number (Wallach and Vu, 1995). However, there is still an ongoing debate about whether leiomyoma has a deleterious effect on conception and reproductive outcome in both natural and assisted reproduction cycles. According to the available data, a large leiomyoma, the presence of a distorted endometrial cavity and/or submucosal localization are more likely to be associated with poor outcome (Klatsky *et al.*, 2008). Nevertheless, there is a paucity of data about whether a single intramural leiomyoma has an adverse effect on assisted reproduction cycles in the presence of a normal endometrial cavity.

As far as is known, no studies have evaluated the impact of a single intramural leiomyoma on intracytoplasmic sperm injection (ICSI) and embryo transfer cycles in which intact endometrium is confirmed by hysteroscopy. The current study compared the ICSI performance of patients having a single leiomyoma with that of controls, with intact endometrium verified in both groups.

Materials and methods

Sixty-one consecutive infertile patients with a single intramural leiomyoma and intact endometrium undergoing ICSI–embryo transfer were retrospectively enrolled from a computerized IVF database. The diagnosis, localization, and size of the leiomyoma

were determined by transvaginal ultrasonography during the early follicular phase of the menstrual cycle. In the leiomyoma group, the exclusion criteria were the presence of any type of endocervical or intrauterine pathology, including endocervical or endometrial polyp, uterine septum, intrauterine synechiae, submucous leiomyoma, distortion of the endometrial cavity detected by transvaginal ultrasonography and/or office hysteroscopy, and history of any uterine surgery including myomectomy. Irrespective of localization, patients with more than one leiomyoma were also excluded.

The control group consisted of 444 age-matched patients undergoing ICSI–embryo transfer without any endocervical or intrauterine pathology revealed by both transvaginal ultrasonography and office hysteroscopy as described above.

In order to confirm the presence of intact endometrium, office hysteroscopy was performed in all participants with a rigid 2.9 mm in diameter scope and 30° telescope (Storz Co., Tuttlingen, Germany) via saline distention on days 6–12 of the menstrual cycle.

All the couples had severe male factor infertility necessitating ICSI using fresh ejaculated spermatozoa. During ovarian stimulation, luteal–long leuprolide acetate (Lucrin; Abbott, Cedex, Istanbul, Turkey) and recombinant FSH (Gonal-F; Serono, Istanbul, Turkey) using the step-down protocol were used. The starting dose of gonadotrophin was determined based on female age, antral follicle count (AFC) at baseline transvaginal ultrasonography, body mass index (BMI) and previous ovarian response, if available. Ovarian response was monitored with frequent serum oestradiol measurements and transvaginal ultrasound. The criterion for HCG (Profasi; Serono, Istanbul, Turkey) administration was the presence of three or more follicles exceeding 17 mm in diameter.

Oocyte retrieval was carried out under local anaesthesia by vaginal ultrasound-guided puncture of follicles 36 h after human chorionic gonadotrophin (HCG) administration. Standard procedures were carried out for gamete–embryo handling and day-3 embryo transfer was performed in all cases using a soft catheter. The luteal phase was supported by daily vaginal progesterone suppositories (Crinone; Serono, Istanbul, Turkey) starting 1 day after oocyte retrieval.

Embryos were graded on day 3 according to a 1–4 scoring system (with 1 being the best), which was based on fragmentation, cell symmetry, and blastomere number (Hardarson *et al.*, 2001). The embryos with even blastomeres and no fragmentation were graded as grade 1, those with even blastomeres and <20% fragmentation as grade 2a, those with uneven blastomeres and no fragmentation as grade 2b, and those with uneven blastomeres and <20% fragmentation as grade 2ab. The embryos with 20–50% fragmentation and >50% fragmentation were graded as grade 3 and 4 embryos respectively (Hardarson *et al.*, 2001). Grades 1–3 were considered transferable embryos. All the embryos were transferred on day 3.

Clinical pregnancy was defined as the presence of an intrauterine gestational sac on transvaginal ultrasound. The implantation rate was defined as the number of gestational sacs observed on transvaginal ultrasound per 100 embryos transferred. Miscarriage was defined by the presence of trophoblastic tissue at dilatation and in the curettage pathology specimen.

The statistical analyses were performed using the Statistical Package for the Social Sciences (ver. 12.0; SPSS Inc., Chicago, USA). Chi-squared and Fisher's exact tests were used to analyse nominal variables in the form of frequency tables. Normally distributed (Kolmogorov–Smirnov test) parametric variables were tested by independent samples *t*-test. Non-normally distributed metric variables were analysed by Mann–Whitney *U*-test, if indicated. $P < 0.05$ was considered statistically significant. Spearman's *rho* test was used to analyse bivariate correlations. Values were expressed as mean ± SD unless otherwise stated.

Since all these cases occurred in routine IVF programme patients in the IVF unit, Institutional Review Board approval was not required.

Results

The mean diameter of the leiomyoma was 16.7 ± 9.9 mm, with a range of 5–43 mm in the leiomyoma group.

Female age, BMI, antral follicle count, duration of stimulation, total dose of FSH used and oestradiol concentration on the day of HCG administration were comparable between the two groups (**Tables 1** and **2**). The mean number of metaphase II oocytes, fertilization rate and mean number of embryos transferred were also similar between the two groups (**Table 3**).

According to the embryological data, the biochemical pregnancy rate per ET was comparable between the leiomyoma and control groups (43 and 42% respectively). The respective figures for the clinical pregnancy rates per ET were 36 and 38% (**Table 3**). The implantation rates were also comparable (**Table 3**). Although the miscarriage rate was higher in the leiomyoma group when compared with the controls, the difference did not reach statistical significance (27 and 19% respectively).

No correlation was noted between the diameter of leiomyoma and the presence of biochemical ($r = –0.185$, not significant) or clinical pregnancy ($r = –0.180$, not significant).

Table 1. Baseline characteristics of leiomyoma and control groups.

Variable	*Leiomyoma group*	*Control group*
No. of patients	61	444
Female age (years)	35.3 ± 4.5	34.5 ± 3.6
Body mass index (kg/m^2)	25.7 ± 4.6	25.8 ± 10.4
Antral follicle count	9.8 ± 5.8	10.5 ± 5.2

Values are expressed as mean ± SD or *n*.
There were no statistically significant differences between the two groups.

Table 2. Ovarian stimulation response of leiomyoma and control groups.

Variable	*Leiomyoma group*	*Control group*
Duration of stimulation (days)	10.1 ± 1.7	10.0 ± 1.9
Total dose of FSH used (IU)	3259 ± 1556	3011 ± 1512
Oestradiol on the day of HCG administration (pg/ml)	2027.1 ± 1333.4	2221.4 ± 1401.4
Endometrial thickness on the day of HCG administration (mm)	10.1 ± 2.5	10.8 ± 2.3

Values are expressed as mean ± SD. HCG = human chorionic gonadotrophin.
There were no statistically significant differences between the two groups.

Table 3. Embryological data and pregnancy outcome of leiomyoma and control groups.

Variable	*Leiomyoma group (n = 61)*	*Control group (n = 444)*
Mean no. of metaphase II oocytes ± SD	8.2 ± 5.4	9.6 ± 6.2
Fertilization rate (%)	355/500 (71)	3055/4246 (72)
Mean no. of embryos transferred ± SD	2.7 ± 1.4	3.0 ± 1.1
Positive β-HCG/embryo transfer (%)	26/61 (43)	186/444 (42)
Clinical pregnancy/embryo transfer (%)	22/61 (36)	167/444 (38)
Implantation rate (%)	33/162 (20)	250/1299 (19)
Miscarriage rate (%)[a]	6/22 (27)	31/167 (19)

[a]Fisher's exact test. HCG = human chorionic gonadotrophin.
There were no statistically significant differences between the two groups.

Discussion

According to a recent systematic review (Klatsky *et al*., 2008), submucosal leiomyoma had the strongest association with poor reproductive outcome. When compared with controls, patients with submucous leiomyomas have lower cumulative pregnancy (12 versus 3%) and implantation rates (30 versus 14%), with higher spontaneous abortion rates (22 versus 47%) (Farhi *et al*., 1995; Eldar-Geva *et al*., 1998; Casini *et al*., 2006; Klatsky *et al*., 2008). Similarly, Pritts *et al*. (2001) reported that 24 patients with submucous myomas undergoing 86 IVF cycles had lower pregnancy (RR 0.30; 95% CI 0.13–0.70) and implantation rates (RR 0.28; 95% CI 0.10--0.72) when compared with infertile controls. The hypothesis that the altered contractility, impaired transport of sperm and/or oocytes, altered endometrial biochemical environment, and local inflammation on endometrium are factors responsible for impaired fertility is not proven.

The available data concerning the effect of intramural leiomyoma on reproductive outcome are more inconclusive. Although earlier controlled studies (Farhi *et al*., 1995; Ramzy *et al*., 1998) described similar reproductive outcomes in patients with intramural leiomyoma, Eldar-Geva *et al*. (1998) reported lower pregnancy (16 versus 31%) and implantation rates (7 versus 12%) in 46 leiomyoma patients when compared with 249 controls. Similarly, Stovall *et al*. (91 leiomyoma patients, 91 controls) indicated that the presence of a uterine leiomyoma with a range of 10–54 mm significantly reduced the chance of a clinical pregnancy or delivery among IVF cycles (Stovall *et al*., 1998).

In a prospective observational study (Hart *et al*., 2001), lower ongoing pregnancy (15 versus 28%) in addition to impaired clinical pregnancy (23 versus 34%) and implantation (12 versus 20%) rates in patients with leiomyomas with a mean diameter of 23 ± 11 mm were noted when 112 patients with leiomyomas were compared with 322 controls. Logistic regression analysis showed that the presence of intramural fibroids was a significant variable affecting the chance of an ongoing pregnancy, even after controlling for the number of embryos available for replacement and increasing age (Hart *et al*., 2001). Within another prospective observational cohort (112 leiomyoma patients, 322 controls), Khalaf *et al*. compared the cumulative performance of patients with leiomyomas with that of controls after three cycles of IVF/ICSI (Khalaf *et al*., 2006). They noted that the pregnancy, ongoing pregnancy, and live birth rates in the leiomyoma group were 24, 19 and 15% compared with 33, 29 and 24% in the control group respectively ($P < 0.05$). After adjusting for confounding variables, Cox regression analysis revealed that the presence of leiomyoma significantly reduced the ongoing pregnancy rate at each cycle of IVF/ICSI by 40% [hazard ratio (HR) = 0.60, 95% CI = 0.36–0.99, $P = 0.048$] and the live birth rate at each cycle by 45% (HR = 0.55, 95% CI = 0.32–0.95, $P = 0.03$) (Khalaf *et al*., 2006).

In addition to poor pregnancy rates among IVF/ICSI cycles, the miscarriage rate seems to be increased in patients with intramural leiomyomas. Benson *et al*. (2001) reported that women with leiomyomas of mean diameter 33 ± 21 mm ($n = 143$) had a higher rate of pregnancy loss when compared with those with normal ($n = 715$) uteruses (14 versus 8%). Interestingly, the loss rate was higher in women with multiple fibroids than in women with a single intramural leiomyoma (24 versus 8%) (Benson *et al*., 2001). Wang and Check (2004) also reported a higher miscarriage rate in 49 patients suffering from leiomyoma with a mean diameter less than 60 mm, but similar pregnancy rates

among 73 ovum donor recipients. In a unique study (Gianaroli *et al.*, 2005), 75 patients (n = 129 cycles) having only inner myometrium fibroids were found to have lower implantation (18 versus 27%) and higher miscarriage rates (40 versus 19%) when compared with 127 controls (n = 129 cycles) without leiomyomas.

In contrast to the above-mentioned studies, there are several reports presenting similar levels of reproductive performance in patients with leiomyomas when compared with controls. In 399 consecutive fresh IVF cycles, Surrey *et al.* (2001) noted a significant decrease in implantation only in patients <40 years old with leiomyomas, in spite of hysteroscopically confirmed endometrium. Similarly, Jun *et al.* (2001) (141 leiomyoma patients, 406 controls) reported that uterine leiomyomas and assisted reproduction treatment outcome were not significantly correlated (OR = 0.73, 95% CI: 0.49–1.19, not significant) after controlling for age and other risk factors. Neither the localization of leiomyomas (intramural versus submucosal/subserosal) nor their size had any significant effect on reproductive outcome (Jun *et al.*, 2001). In concordance, Oliveira *et al.* (2004) reported that there was no correlation between location and number of uterine fibroids and the outcomes of IVF–ICSI. However, patients with intramural fibroids >40 mm had lower pregnancy rates than those with intramural fibroids ≤4–20 and 21–40 mm (29 versus 53 and 51%). Therefore, they recommended caution concerning patients with fibroids >40 mm and that those patients should undergo treatment before they are enrolled in IVF–ICSI cycles (Oliveira *et al.*, 2004). In a recent study, Klatsky *et al.* (2007) also failed to find any deleterious effect in the context of reproductive outcome in patients with non-cavity-distorting large (40–80 mm) and multiple leiomyomas (94 leiomyoma patients, 275 controls).

In a previous report from the study centre (Yarali and Bukulmez, 2002), the effect of intramural and subserous leiomyomas on ICSI was evaluated in a retrospective case–control study of 108 women with uterine fibroids and 324 controls. Seventy-three women had intramural and 35 women had subserous fibroids and the maximum diameter in any patient ranged from 5 to 100 mm. The number of fibroids in a patient ranged from one to eight. The first cycle outcome was compared with 324 age and body mass index matched ICSI patients/cycles. The ICSI cycles of patients with intramural and subserous leiomyoma were comparable in terms of implantation and clinical pregnancy rates (Yarali and Bukulmez, 2002). Similarly, in the present study, no deleterious effect of a single intramural leiomyoma on reproductive outcome was observed in ICSI cycles when normal endometrial structure was confirmed by hysteroscopy.

Since the effect of intramural leiomyomas on reproductive outcome is not clear, the validity of myomectomy in patients undergoing IVF is still under debate. Although some authors have reported improved reproductive performance including higher pregnancy (16–57%) and lower miscarriage rates, most of them are based on uncontrolled and retrospective observations (Babaknia *et al.*, 1978; Berkeley *et al.*, 1983; Gehlbach *et al.*, 1993). In fact, there is a paucity of data about which diameter and number of leiomyomas should be taken as the threshold indicating surgery before IVF. In agreement with Klatsky *et al.* (2007), it appears that unless a randomized controlled study comparing myomectomy with conservative management is performed, recommending routine surgical removal of intramural leiomyomas that do not distort the cavity should be avoided.

In patients with leiomyomas, medical treatment is generally recommended to be prescribed in the treatment of perimenopausal women who anticipate a reduction in symptoms when they ultimately become menopausal (Practice Committee of the American Society for Reproductive Medicine, 2006). Although medical treatment alone cannot be recommended for younger women, who will require some type of definitive therapy, it may be employed before myomectomy, particularly in patients suffering from anaemia (Felberbaum *et al.*, 2001).

The inconsistency among the available data may be due to the heterogeneous pool of data, which may be related to the following factors among the studies: (i) the mean diameter of the leiomyoma is distinct in each study with a range of 4–100 mm; (ii) more than one leiomyoma with the combination of more than one localization is encountered in the majority of the trials, which may be a confounding factor; (iii) the endometrial distortion and other confounding endometrial pathologies such as endocervical/endometrial polyp, endometrial synechiae, and endometritis are excluded by only transvaginal ultrasonography in the vast majority of the studies, whereas hysteroscopy is regarded as the gold standard in the evaluation of endometrial integrity (Bettocchi *et al.*, 2004); and (iv) the absence of endometrial evaluations with hysteroscopy to rule out endometrial and/or endocervical disorders among the control group in order to create an optimal control group.

In the present study, the aim was to evaluate the impact of a single intramural leiomyoma in patients with hysteroscopically intact endometrium on ICSI outcome when compared with patients without leiomyomas and healthy endometrium. The main priority of the study is the utilization of office hysteroscopy in all patients with leiomyomas, in order to confirm intact endometrium. With the exception of Surrey *et al.* (2001), previous investigators had relied on ultrasonography alone (Eldar-Geva *et al.*, 1998) or in combination with hysterosalpingography and/or hysteroscopy (Stovall *et al.*, 1998; Jun *et al.*, 2001; Oliveira *et al.*, 2004; Khalaf *et al.*, 2006; Klatsky *et al.*, 2007) to rule out endometrial distortion due to intramural leiomyoma. When compared with other imaging technologies such as transvaginal ultrasonography and saline infusion sonography, there is a paucity of data about the superiority of office hysteroscopy in determining endometrial distortion in cases of intramural leiomyoma. However, despite no abnormality being found with these tools, several subtle intrauterine pathologies such as endometrial and/or endocervical polyp, endometrial synechiae, and endometritis may be noted at hysteroscopy in 18–50% of patients undergoing IVF (Shamma *et al.*, 1992; Wang *et al.*, 1996; Doldi *et al.*, 2005; Bozdag *et al.*, 2008). This may lead to misleading information about the detection of 'non-obvious' endometrial pathologies that may interfere with pregnancy outcome in both the leiomyoma and control groups. The secondary advantage of the data is the examination of only individuals with a single intramural leiomyoma, which may exclude the combined effect of multiple leiomyomas. Due to the retrospective nature of the study, data were not available for the distance of the leiomyoma from the endometrial cavity. The small size and retrospective nature of the study are drawbacks.

It is concluded that, as the integrity of endometrium is verified by hysteroscopy, the clinical pregnancy, implantation, and miscarriage rates are similar in patients with a single intramural leiomyoma when compared with controls. In this respect, although it cannot be recommended routinely, hysteroscopy may be performed in selected patients suffering from leiomyomas in order to verify intact endometrium before IVF/ICSI.

References

Babaknia A, Rock JA, Jones HW Jr 1978 Pregnancy success following abdominal myomectomy for infertility. *Fertility and Sterility* **30**, 644–647.

Benson CB, Chow JS, Chang-Lee W *et al*. 2001 Outcome of pregnancies in women with uterine leiomyomas identified by sonography in the first trimester. *Journal of Clinical Ultrasound* **29**, 261–264.

Berkeley AS, DeCherney AH, Polan ML 1983 Abdominal myomectomy and subsequent fertility. *Surgery, Gynecology and Obstetrics* **156**, 319–322.

Bettocchi S, Nappi L, Ceci O *et al*. 2004 Office hysteroscopy. *Obstetrics and Gynecology Clinics of North America* **31**, 641–654, xi.

Bozdag G, Aksan G, Esinler I *et al*. 2008 What is the role of office hysteroscopy in women with failed IVF cycles? *Reproductive BioMedicine Online* **17**, 410–415.

Casini ML, Rossi F, Agostini R *et al*. 2006 Effects of the position of fibroids on fertility. *Gynecological Endocrinology* **22**, 106–109.

Doldi N, Persico P, Di Sebastiano F *et al*. 2005 Pathologic findings in hysteroscopy before in vitro fertilization–embryo transfer (IVF–ET). *Gynecological Endocrinology* **21**, 235–237.

Eldar-Geva T, Meagher S, Healy DL *et al*. 1998 Effect of intramural, subserosal, and submucosal uterine fibroids on the outcome of assisted reproductive technology treatment. *Fertility and Sterility* **70**, 687–691.

Farhi J, Ashkenazi J, Feldberg D *et al*. 1995 Effect of uterine leiomyomata on the results of in-vitro fertilization treatment. *Human Reproduction* **10**, 2576–2578.

Felberbaum RE, Kupker W, Krapp M *et al*. 2001 Preoperative reduction of uterine fibroids in only 16 days by administration of a gonadotrophin-releasing hormone antagonist (Cetrotide). *Reproductive BioMedicine Online* **3**, 14–18.

Gehlbach DL, Sousa RC, Carpenter SE *et al*. 1993 Abdominal myomectomy in the treatment of infertility. *International Journal of Gynaecology and Obstetrics* **40**, 45–50.

Gianaroli L, Gordts S, D'Angelo A *et al*. 2005 Effect of inner myometrium fibroid on reproductive outcome after IVF. *Reproductive BioMedicine Online* **10**, 473–477.

Hardarson T, Hanson C, Sjogren A *et al*. 2001 Human embryos with unevenly sized blastomeres have lower pregnancy and implantation rates: indications for aneuploidy and multinucleation. *Human Reproduction* **16**, 313–318.

Hart R, Khalaf Y, Yeong CT *et al*. 2001 A prospective controlled study of the effect of intramural uterine fibroids on the outcome of assisted conception. *Human Reproduction* **16**, 2411–2417.

Jun SH, Ginsburg ES, Racowsky C *et al*. 2001 Uterine leiomyomas and their effect on in vitro fertilization outcome: a retrospective study. *Journal of Assisted Reproduction and Genetics* **18**, 139–143.

Khalaf Y, Ross C, El-Toukhy T *et al*. 2006 The effect of small intramural uterine fibroids on the cumulative outcome of assisted conception. *Human Reproduction* **21**, 2640–2644.

Klatsky PC, Tran ND, Caughey AB *et al*. 2008 Fibroids and reproductive outcomes: a systematic literature review from conception to delivery. *American Journal of Obstetrics and Gynecology* **198**, 357–366.

Klatsky PC, Lane DE, Ryan IP *et al*. 2007 The effect of fibroids without cavity involvement on ART outcomes independent of ovarian age. *Human Reproduction* **22**, 521–526.

Oliveira FG, Abdelmassih VG, Diamond MP *et al*. 2004 Impact of subserosal and intramural uterine fibroids that do not distort the endometrial cavity on the outcome of in vitro fertilization–intracytoplasmic sperm injection. *Fertility and Sterility* **81**, 582–587.

Practice Committee of the American Society for Reproductive Medicine. 2006 Myomas and reproductive function. *Fertility and Sterility* **86**, S194–S199.

Pritts EA 2001 Fibroids and infertility: a systematic review of the evidence. *Obstetrical and Gynecological Survey* **56**, 483–491.

Ramzy AM, Sattar M, Amin Y *et al*. 1998 Uterine myomata and outcome of assisted reproduction. *Human Reproduction* **13**, 198–202.

Shamma FN, Lee G, Gutmann JN *et al*. 1992 The role of office hysteroscopy in in vitro fertilization. *Fertility and Sterility* **58**, 1237–1239.

Stovall DW, Parrish SB, Van Voorhis BJ *et al*. 1998 Uterine leiomyomas reduce the efficacy of assisted reproduction cycles: results of a matched follow-up study. *Human Reproduction* **13**, 192–197.

Surrey ES, Lietz AK, Schoolcraft WB 2001 Impact of intramural leiomyomata in patients with a normal endometrial cavity on in vitro fertilization–embryo transfer cycle outcome. *Fertility and Sterility* **75**, 405–410.

Wallach EE, Vu KK 1995 Myomata uteri and infertility. *Obstetrics and Gynecology Clinics of North America* **22**, 791–799.

Wang CW, Lee CL, Lai YM *et al*. 1996 Comparison of hysterosalpingography and hysteroscopy in female infertility. *Journal of the American Association of Gynecologic Laparoscopists* **3**, 581–584.

Wang W, Check JH 2004 Effect of corporal fibroids on outcome following embryo transfer in donor–oocyte recipients. *Clinical and Experimental Obstetrics and Gynecology* **31**, 263–264.

Yarali H, Bukulmez O 2002 The effect of intramural and subserous uterine fibroids on implantation and clinical pregnancy rates in patients having intracytoplasmic sperm injection. *Archives of Gynecology and Obstetrics* **266**, 30–33.

Declaration: The authors report no financial or commercial conflicts of interest.

Received 28 September 2008; refereed 23 October 2008; accepted 9 March 2009.